REMARKS

Claims 1-20 are pending in the application. Claim 1 is currently amended.

The present claims address methods and materials that share a gene construct. The gene construct contains a positive selectable marker and a negative selectable marker. Claim 1 has been amended to recite respective characteristics of the positive and negative markers, namely, that they differ in kind and function with complementary positive and negative selection media when transformed into cells. The complementary relationship is described, for example, in paragraph 30 of the Specification where a positive marker facilitates growth and a negative marker hinders growth.

Claims 18 and 20 has been amended to insert the work "is" after plant. This amendment is made to correct a typographical error.

The claimed features are particularly advantageous in producing genetically modified plants where the dual selection process is accompanied by a looping-out of both marker genes for a final selection of plants that simply contain a gene of interest (see paragraphs 18 and 35). This advantage alleviates environmental concerns where the marker genes are unnecessarily inserted by prior technologies.

A substitute Declaration accompanies this response.

The amendment to claims 18 and 20 overcomes the objection to these claims by inserting the verb "is."

Claims 1, 4-6, 8, 10, 12, 14, 15, and 17-20 stand rejected under 35 U.S.C. §112 first paragraph as failing to comply with the written description requirement. The Office cites various cases including *Vas-Cath*, 19 USPQ2d 1111, and *Lilly* 43 USPQ2d at 1406 for the propositions that the specification must show to those skilled in the art that Applicant possessed the invention at the time of filing and that it is not sufficient to claim structure that is supported by mere function alone. As per *Lilly*, a claim that recites a genus of functionality, there must be adequate support in the specification relating structure or some rationale to the functionality.

The issue presently is that the Office deems the phrase "negative selectable marker" as being unsupported by a sufficient number of specifically disclosed markers or a rationale relating the sequence of DNA to this functionality. *Koprek*, Plant Journal (1999) 19(6), 719-726 is cited as showing that a broad spectrum of negative selectable marker genes was not conventional in the art at the time the application was filed.

We take extreme objection to this characterization of *Koprek* because negative selection markers are well known in the art—in fact it is a term of art. The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and

already available to the public. *In re Bucher*, 929 F.2d 660, 661 (Fed. Cir. 1991). The Introduction section of *Koprek* cites no fewer than 15 instances of negative selectable markers including at least: Mariani et al., 1992; Renckens et al. 1992; Thykjaer et al. 1997; Strittmatter et al. 1995; Koltunow et al., 1990; Czako et al. 1992; Koning et al. 1992; Xiang and Guerra 1993; Depicker et al. 1988; Karlin-Neuman et al., 1991; Beclin et al., 1993; Czako and Marton, 1994; Kobayashi et al., 1995; Perera et al., 1993; Stougaard 1993; Shclaman and Hooykaas, 1997; Stougaard, 1993; and O'Keefe et al., 1991, 1993, 1994. The References section of that article cites even more (34) such articles. What the Office has taken as evidence of unconventionality is merely an exhortation to develop more of these markers in a field that already has so many of them.

Despite the Office's frequent reliance upon *Lilly* as a bright line prohibition against functional recitations in biotechnology claims, the Federal Circuit has itself distinguished Lilly to hold that such claims are permitted under appropriate circumstances, such as where the art is sufficiently advanced to associate structure with function. *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 at 1613 (Fed. Cir. 2002) (noting that the state of antibody art is sufficiently advanced and mature). Given the widespread knowledge about this genus of markers, it is sufficient that Applicant has disclosed *CodA* and *dhlA*.

In Lilly, the primary concern was whether the disclosed sequence for rat insulin—an insulin gene being entirely new—was sufficient to support a claim for all vertebrate insulin or all mammalian insulin. That is distinct from the present case where the negative selection marker art is relatively advanced. The present situation is one that is more analogous *In re Angstadt and Griffin*, (CCPA) 190 USPQ 214, where the court held that to limit an Applicant's protection to only those species explicitly disclosed in a specification would undermine the intent of the Patent Act and discourage inventors from filing patent applications, especially in unpredictable arts. The case, which involved catalysts for the production of hydroperoxides, is quoted below:

> Appellants have apparently not disclosed *every* catalyst which will work; they have apparently not disclosed *every* catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with *every* species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used in "forming hydroperoxides."

The nature and advantage of the presently claimed invention does not hinge upon use of a particular negative selection marker among a variety of known markers that may be used, and so the claims are commensurate with the scope of the invention. For the reasons explained above, we request reconsideration and withdrawal of the §112 first paragraph rejection.

Claims 1 and 4 stand rejected under 35 U.S.C. §102(e) over U>S. Patent No. 6,051,431 to Selten. Selten shows use of a single negative selection marker that may be repeated. Because the admS negative selection marker may also be used as a positive selection marker and the unit repeats, the Office finds that both a negative and a positive marker are in place. This type of arrangement would not work for the present purpose where the selection process is to delete both of the markers by the aforementioned natural looping processes. Selten would not work well for this purpose because, in essence, both negative and positive selections would be for the same marker. Amended claim 1 distinguishes Selten in a nonobvious way be reciting that the negative and positive selection markers differ in kind. Here we also note that Selten's replicated portions of the glaA gene are from a nonocoding region that does not function as a positive or negative selection marker. Claim 4 incorporates the limitations of claim 1 and is likewise allowable.

Based upon the foregoing discussion, Applicant's attorney submits that the amended claims are allowable and respectfully solicits a Notice of Allowance.

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